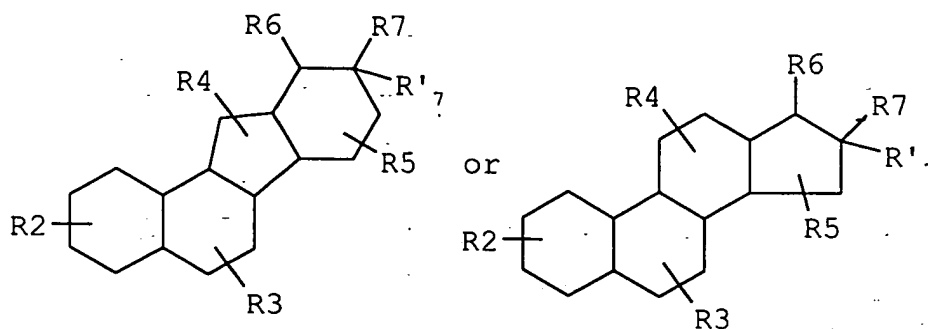


We claim:

1. A method for inhibiting an altered growth state of a cell having a *ptc* loss-of-function phenotype or a *smoothened* gain-of-function phenotype, comprising contacting the cell with a *ptc* agonist in a sufficient amount to inhibit the altered growth state, wherein the *ptc* agonist is a organic molecule having a molecular weight less than about 750 amu.
2. A method for inhibiting aberrant proliferation of a cell having a *ptc* loss-of-function phenotype or a *smoothened* gain-of-function phenotype comprising contacting the cell with a *ptc* agonist in a sufficient amount to inhibit proliferation of the cell.
3. The method of claim 1, wherein the *ptc* agonist causes repression of *smoothened*-mediated signal transduction.
4. The method of claim 1, wherein the *ptc* agonist is a steroidal alkaloid.
5. The method of claim 4, wherein the steroidal alkaloid is represented in the general formulas (I), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula I.

wherein, as valence and stability permit,

$R_2$ ,  $R_3$ ,  $R_4$ , and  $R_5$ , represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxy, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ;

$R_6$ ,  $R_7$ , and  $R'_7$ , are absent or represent, independently, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxy, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ , or

$R_6$  and  $R_7$ , or  $R_7$  and  $R'_7$ , taken together form a ring or polycyclic ring, e.g., which is substituted or unsubstituted,

with the proviso that at least one of  $R_6$ ,  $R_7$ , or  $R'_7$  is present and includes a primary or secondary amine;

$R_8$  represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle; and

$m$  is an integer in the range 0 to 8 inclusive.

6. The method of claim 5, wherein:

$R_2$  and  $R_3$ , for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)- $R_8$ ;

$R_4$ , for each occurrence, is an absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)- $R_8$ ;

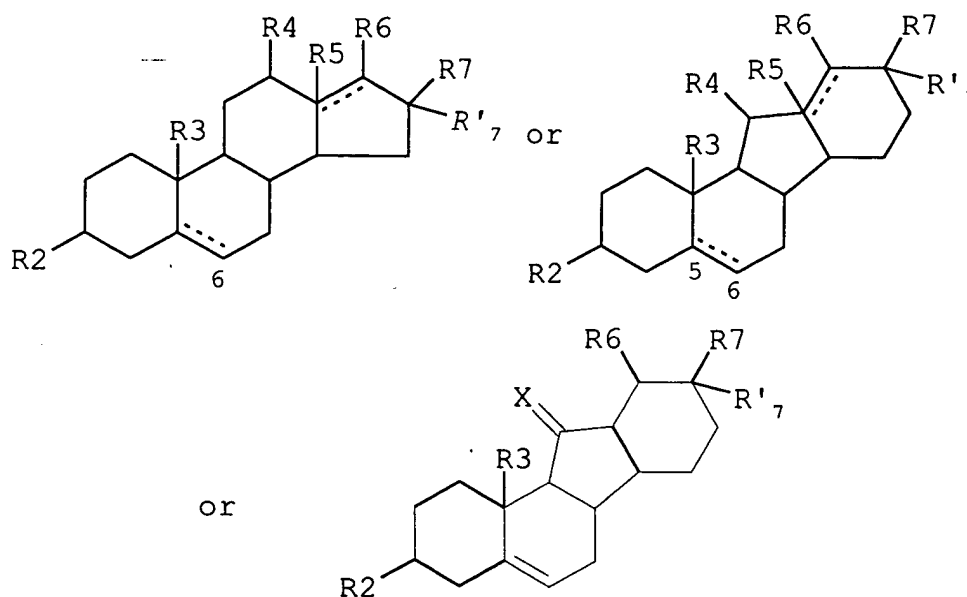
$R_6$ ,  $R_7$ , and  $R'_7$  each independently represent, hydrogen, alkyls, alkenyls, alkynyls, amines, imines, amides, carbonyls, carboxyls, carboxamides, ethers, thioethers, esters, or  $-(CH_2)_m-R_8$ , or

$R_7$ , and  $R'_7$  taken together form a furanopiperidine, such as perhydrofuro[3,2-b]pyridine, a pyranopiperidine, a quinoline, an indole, a pyranopyrrole, a naphthyridine, a thiofuranopiperidine, or a thiopyranopiperidine

with the proviso that at least one of  $R_6$ ,  $R_7$ , or  $R'_7$  is present and includes a primary or secondary amine;

$R_8$  represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle, and preferably  $R_8$  is a piperidine, pyrimidine, morpholine, thiomorpholine, pyridazine,

7. The method of claim 4, wherein the steroidal alkaloid is represented in the general formula (II), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula II

wherein

$R_2$ ,  $R_3$ ,  $R_4$ , and  $R_5$ , represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl,  $=O$ ,  $=S$ , alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ;

$R_6$ ,  $R_7$ , and  $R'_7$ , are absent or represent, independently, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl,  $=O$ ,  $=S$ , alkoxyl, silyloxy, amino, nitro, thiol,

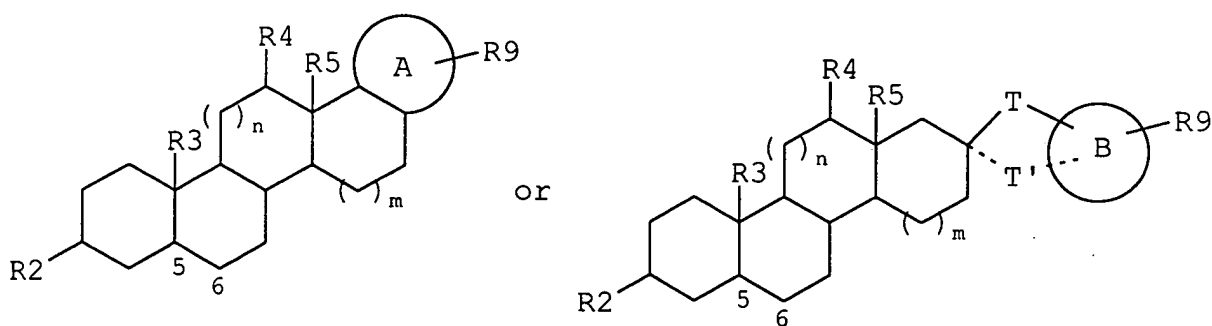
amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ , or

$R_6$  and  $R_7$ , or  $R_7$  and  $R'_7$ , taken together form a ring or polycyclic ring, e.g., which is substituted or unsubstituted,

with the proviso that at least one of  $R_6$ ,  $R_7$ , or  $R'_7$  is present and includes a primary or secondary amine;

X represents O or S, though preferably O.

8. The method of claim 4, wherein the steroidal alkaloid is represented in the general formula (III), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula III

wherein

$R_2$ ,  $R_3$ ,  $R_4$ , and  $R_5$ , represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl,  $=O$ ,  $=S$ , alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ;

$R_8$  represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle; and

A and B represent monocyclic or polycyclic groups;

T represent an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, ether or amine linkage of 1-10 bond lengths;

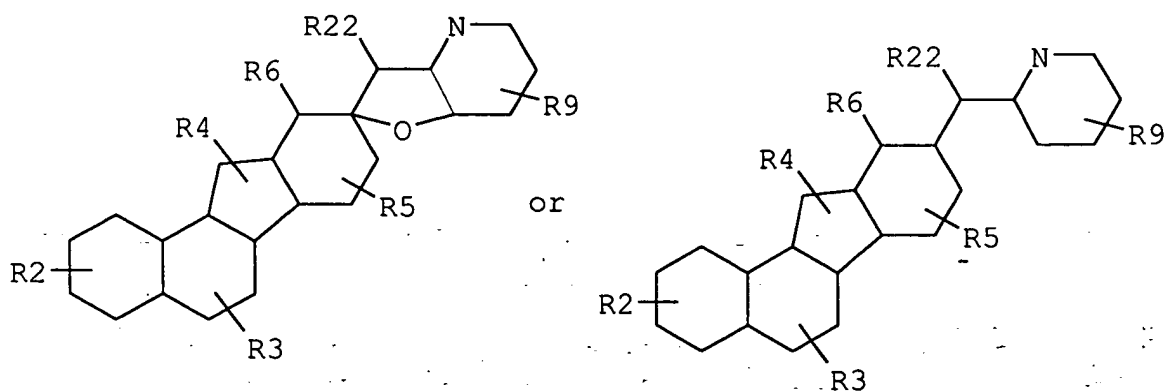
T' is absent, or represents an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, ether or amine linkage of 1-3 bond lengths, wherein if T and T' are present together, than T and T' taken together with the ring A or B form a covalently closed ring of 5-8 ring atoms;

R<sub>9</sub> represent one or more substitutions to the ring A or B, which for each occurrence, independently represent halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ; and

n and m are, independently, zero, 1 or 2;

with the proviso that A and R<sub>9</sub>, or T, T' B and R<sub>9</sub>, taken together include at least one primary or secondary amine.

9. The method of claim 4, wherein the steroidal alkaloid is represented in the general formula (IV), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula IV

wherein

R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub>, represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy,

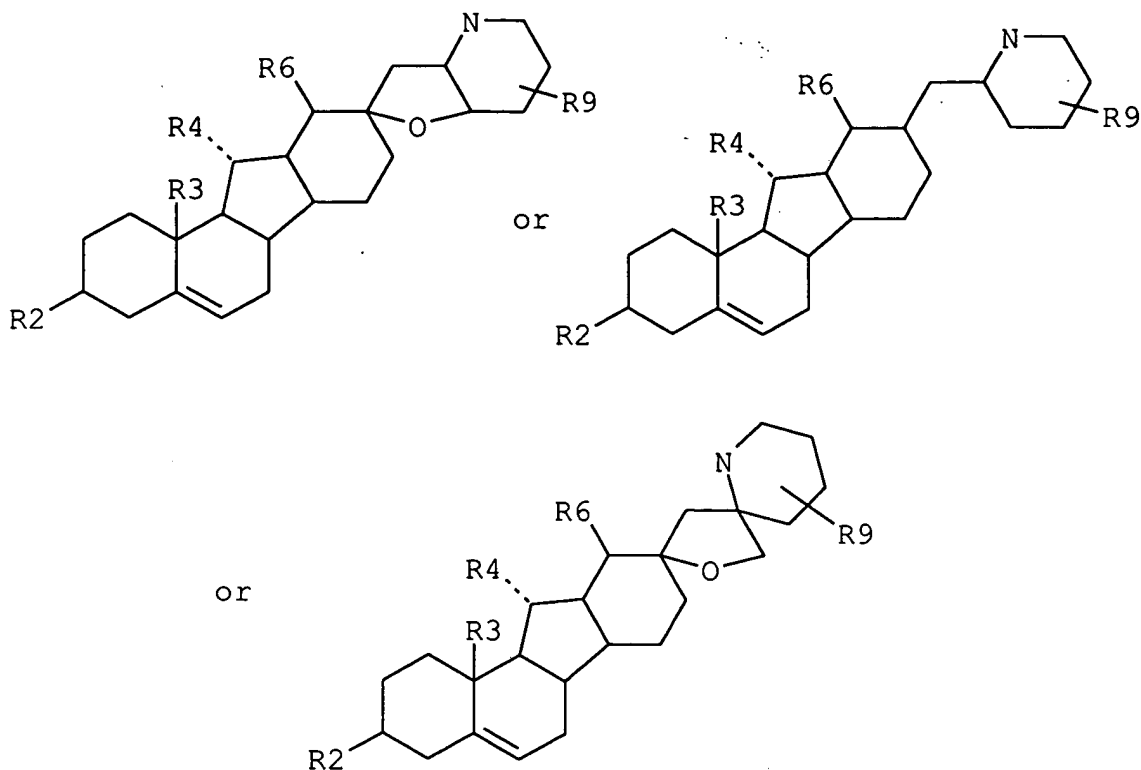
amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ;

$R_6$  is absent or represent, independently, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl,  $=O$ ,  $=S$ , alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ;

$R_9$  represent one or more substitutions to the ring A or B, which for each occurrence, independently represent halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl,  $=O$ ,  $=S$ , alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ; and

$R_{22}$  is absent or represents an alkyl, an alkoxyl or  $-OH$ .

10. The method of claim 4, wherein the steroidal alkaloid is represented in the general formula (V) or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:

Formula V

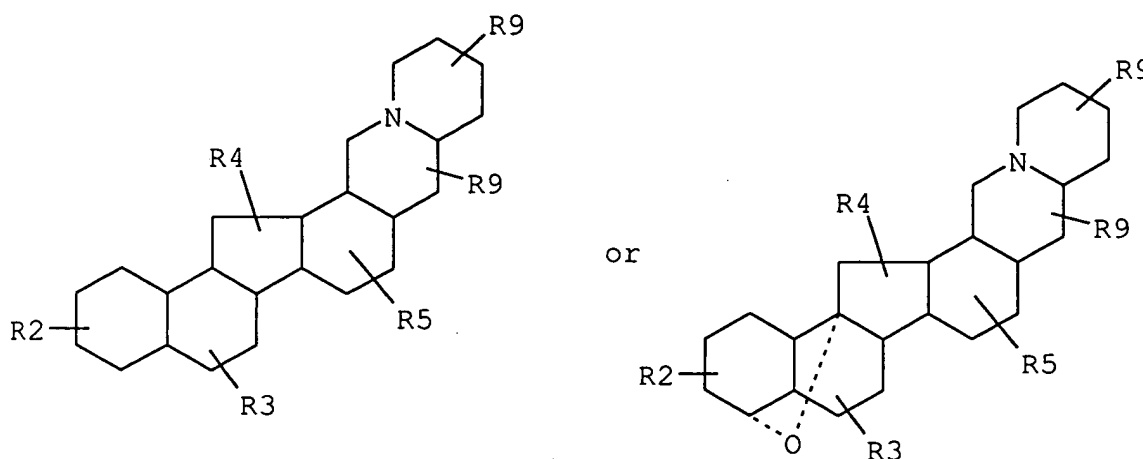
$R_2$ ,  $R_3$ ,  $R_4$ , and  $R_5$ , represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxy, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ;

$R_6$  is absent or represent, independently, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxy, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ; and

$R_9$  represent one or more substitutions to the ring A or B, which for each occurrence, independently represent halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxy, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides,

anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ .

11. The method of claim 4, wherein the steroidal alkaloid is represented in the general formula (VI), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



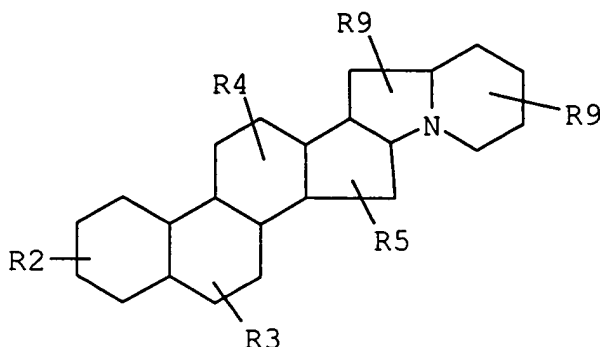
Formula VI

wherein

$R_2$ ,  $R_3$ ,  $R_4$ , and  $R_5$ , represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl,  $=O$ ,  $=S$ , alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ; and

$R_9$  represent one or more substitutions to the ring A or B, which for each occurrence, independently represent halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl,  $=O$ ,  $=S$ , alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ .

12. The method of claim 4, wherein the steroidal alkaloid is represented in the general formula (VII) or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula VII

wherein

$R_2$ ,  $R_3$ ,  $R_4$ , and  $R_5$ , represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ; and

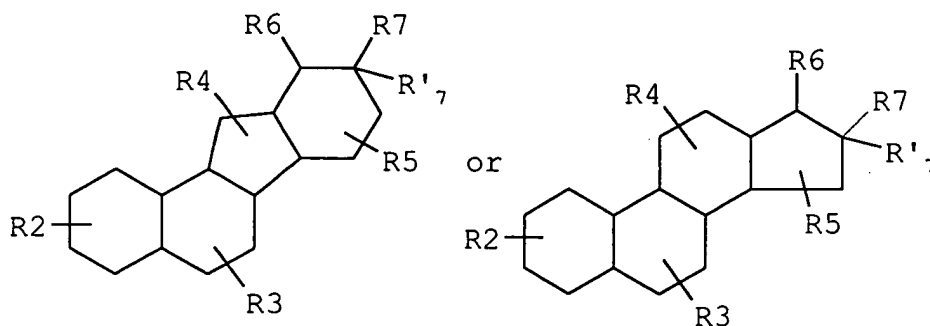
$R_9$  represent one or more substitutions to the ring A or B, which for each occurrence, independently represent halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ .

13. The method of claim 4, wherein the steroidal alkaloid does not substantially interfere with the biological activity of such steroids as aldosterone, androstane, androstene, androstenedione, androsterone, cholecalciferol, cholestane, cholic acid, corticosterone, cortisol, cortisol acetate, cortisone, cortisone acetate, deoxycorticosterone, digitoxigenin, ergocalciferol, ergosterol, estradiol-17- $\alpha$ , estradiol-17- $\beta$ , estriol, estrane, estrone, hydrocortisone, lanosterol, lithocholic

acid, mestranol,  $\beta$ -methasone, prednisone, pregnane, pregnenolone, progesterone, spironolactone, testosterone, triamcinolone and their derivatives.

14. The method of claim 4, wherein the steroidal alkaloid does not specifically bind a nuclear hormone receptor.
15. The method of claim 4, wherein the steroidal alkaloid does not specifically bind estrogen or testosterone receptors.
16. The method of claim 4, wherein the steroidal alkaloid has no estrogenic activity at therapeutic concentrations.
17. The method of claim 1, wherein the *ptc* agonist inhibits *ptc* loss-of-function or *smoothened* gain-of-function mediated signal transduction with an ED<sub>50</sub> of 1mM or less.
18. The method of claim 1, wherein the *ptc* agonist inhibits *ptc* loss-of-function or *smoothened* gain-of-function mediated signal transduction with an ED<sub>50</sub> of 1 $\mu$ M or less.
19. The method of claim 1, wherein the *ptc* agonist inhibits *ptc* loss-of-function or *smoothened* gain-of-function mediated signal transduction with an ED<sub>50</sub> of 1nM or less.
20. The method of claim 1, wherein the cell is contacted with the *ptc* agonist *in vitro*.
21. The method of claim 1, wherein the cell is contacted with the *ptc* agonist *in vivo*.
22. The method of claim 1, wherein the *ptc* agonist is administered as part of a therapeutic or cosmetic application.

23. The method of claim 22, wherein the therapeutic or cosmetic application is selected from the group consisting of regulation of neural tissues, bone and cartilage formation and repair, regulation of spermatogenesis, regulation of smooth muscle, regulation of lung, liver and other organs arising from the primitive gut, regulation of hematopoietic function, regulation of skin and hair growth, etc.
24. A pharmaceutical preparation comprising a steroidal alkaloid represented in the general formulas (I), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula I

wherein, as valence and stability permit,

R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub>, represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ ;

R<sub>6</sub>, R<sub>7</sub>, and R'<sub>7</sub>, are absent or represent, independently, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or  $-(CH_2)_m-R_8$ , or

R<sub>6</sub> and R<sub>7</sub>, or R<sub>7</sub> and R'<sub>7</sub>, taken together form a ring or polycyclic ring, e.g., which is substituted or unsubstituted,

with the proviso that at least one of R<sub>6</sub>, R<sub>7</sub>, or R'<sub>7</sub> is present and includes a primary or secondary amine;

R<sub>g</sub> represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle; and

m is an integer in the range 0 to 8 inclusive.

25. A method for inhibiting an altered growth state of a cell having a *ptc* loss-of-function phenotype, *hedgehog* gain-of-function phenotype, or a *smoothened* gain-of-function phenotype, comprising contacting the cell with a composition including at least one cAMP agonist.
26. The method of claim 25, wherein at least one cAMP agonist activates adenylate cyclase.
27. The method of claim 25, wherein at least one cAMP agonist is a cAMP analog.
28. The method of claim 25, wherein at least one cAMP agonist is a cAMP phosphodiesterase inhibitor.
29. The method of claim 25, wherein the composition inhibits *ptc* loss-of-function, *hedgehog* gain-of-function, or *smoothened* gain-of-function mediated signal transduction with an ED<sub>50</sub> of 1 mM or less.
30. The method of claim 25, wherein the composition inhibits *ptc* loss-of-function, *hedgehog* gain-of-function, or *smoothened* gain-of-function mediated signal transduction with an ED<sub>50</sub> of 1 μM or less.
31. The method of claim 25, wherein the composition inhibits *ptc* loss-of-function, *hedgehog* gain-of-function, or *smoothened* gain-of-function mediated signal transduction with an ED<sub>50</sub> of 1 nM or less.

32. The method of claim 25, wherein the cell is contacted with the composition *in vitro*.
33. The method of claim 25, wherein the cell is contacted with the composition *in vivo*.
34. The method of claim 25, wherein the composition is administered as part of a therapeutic or cosmetic application.
35. The method of claim 34, wherein the therapeutic or cosmetic application is selected from the group consisting of regulation of neural tissues, bone and cartilage formation and repair, regulation of spermatogenesis, regulation of smooth muscle, regulation of lung, liver and other organs arising from the primitive gut, regulation of hematopoietic function, regulation of skin and hair growth, etc.
36. The method of claim 25, wherein the composition includes forskolin or a derivative thereof.
37. A method for treating or preventing basal cell carcinoma, comprising administering a composition including a cAMP agonist to a patient in an amount sufficient to inhibit progression of basal cell carcinoma.
38. A method for inhibiting an altered growth state of a cell having a *ptc* loss-of-function phenotype, *hedgehog* gain-of-function phenotype, or a *smoothened* gain-of-function phenotype, comprising
  - determining the phenotype of the cell; and
  - if the phenotype is a *ptc* loss-of-function, *hedgehog* gain-of-function, or a *smoothened* gain-of-function phenotype, treating the cell with a cAMP agonist in an amount sufficient to inhibit the altered growth state of the cell.